

**WHAT IS CLAIMED IS:**

1. A nucleic acid composition comprising a plurality of sets of nucleic acid molecules, each nucleic acid molecule encoding a human immunodeficiency virus (HIV) envelope glycoprotein, wherein each set of nucleic acid molecules encodes a different type of HIV envelope glycoprotein, or comprises a primary isolate sequence from a distinct genetic clade.
2. The nucleic acid composition of claim 1, wherein the nucleic acids comprise DNA plasmids.
3. The nucleic acid composition of claim 1, wherein the HIV envelope glycoprotein is any one or more of gp120, gp140, gp160, and gp41.
4. The nucleic acid composition of claim 1, further comprising a set of nucleic acid molecules encoding a HIV gag protein.
5. The nucleic acid composition of claim 1, wherein the envelope glycoprotein of one or more of the plurality of sets is a HIV-1 envelope glycoprotein.
6. The nucleic acid composition of claim 1, wherein the envelope glycoprotein of one or more of the plurality of sets is a gp120 envelope glycoprotein.
7. The nucleic acid composition of claim 1, wherein the envelope glycoprotein of one or more of the plurality of sets is from a clade of a major (M) group of clades.
8. The nucleic acid composition of claim 7, wherein the clade is clade A, B, C, D, E, F, G, H, I, J, or K.
9. The nucleic acid composition of claim 1, wherein the envelope glycoprotein of one or more of the plurality of sets is from a clade of an outlier (O) group of clades.

10. The nucleic acid composition of claim 1, wherein the envelope glycoprotein of one or more of the plurality of sets is from a clade of an N group of clades.
11. The nucleic acid composition of claim 8, wherein the clade is clade B.
12. The nucleic acid composition of claim 8, wherein the envelope glycoprotein is an envelope glycoprotein of a B715 isolate.
13. The nucleic acid composition of claim 8, wherein the clade is clade C.
14. The nucleic acid composition of claim 1, wherein one or more of the sets of nucleic acids comprises optimized codons.
15. A nucleic acid composition comprising a plurality of sets of nucleic acid molecules, wherein the plurality comprises two or more of the following sets:
  - a set of nucleic acid molecules, each encoding a human immunodeficiency virus (HIV) envelope glycoprotein of clade A;
  - a set of nucleic acid molecules, each encoding a HIV envelope glycoprotein of clade B;
  - a set of nucleic acid molecules, each encoding a HIV envelope glycoprotein of clade C; and
  - a set of nucleic acid molecules, each encoding a HIV envelope glycoprotein of clade E;wherein each set of nucleic acid molecules encodes a primary isolate sequence of the envelope glycoprotein.
16. The composition of claim 15, wherein the composition comprises one of each set.
17. The composition of claim 15, further comprising a set of nucleic acid molecules encoding a human immunodeficiency virus (HIV) gag protein, wherein the set encodes a primary isolate sequence of the gag protein.

18. The composition of claim 17, wherein the gag protein is a gag protein of clade C.
19. The composition of claim 17, wherein the gag protein is a gag protein of clade B.
20. The composition of claim 1, wherein the composition comprises between 50 µg and 2,500 µg of nucleic acid of each set.
21. A pharmaceutical composition comprising a composition of claim 1 and a pharmaceutically acceptable excipient.
22. A method of treating an individual with Acquired Immune Deficiency Syndrome (AIDS), the method comprising administering to the individual an amount of the pharmaceutical composition of claim 21 sufficient to inhibit disease progression due to human immunodeficiency virus (HIV).
23. The method of claim 22, wherein the mode of administration is selected from the group consisting of topical administration, oral administration, injection by needle, needleless jet injection, intradermal administration, intramuscular administration, and gene gun administration.
24. The method of claim 22, wherein the immune response is a protective immune response.
25. The method of claim 22, wherein the immune response is a cell-mediated immune response.
26. The method of claim 22, wherein the immune response is a humoral immune response.

27. The method of claim 22, wherein the immune response is a cell-mediated immune response and a humoral immune response.
28. The method of claim 22, wherein the composition is administered in combination with a second therapy for HIV infection.
29. The method of claim 28, wherein the second therapy for HIV infection comprises therapy with a nucleoside reverse transcriptase inhibitor, therapy with a non-nucleoside reverse transcriptase inhibitor, or therapy with a HIV protease inhibitor.
30. The method of claim 28, wherein the second therapy for HIV infection comprises therapy with a nucleoside reverse transcriptase inhibitor, therapy with a non-nucleoside reverse transcriptase inhibitor, and therapy with a HIV protease inhibitor.
31. A method of inducing an immune response against human immunodeficiency virus (HIV) or an HIV epitope in a vertebrate mammal, the method comprising:  
administering to the mammal an amount of the composition of claim 1 sufficient to elicit an immune response against HIV or an HIV epitope in the vertebrate mammal.
32. The method of claim 31, further comprising isolating immune cells from the vertebrate mammal; and testing an immune response of the isolated immune cells in vitro.
33. The method of claim 31, wherein the composition is administered in multiple doses over an extended period of time (e.g., over a period of 4 weeks or more).
34. The method of claim 31, further comprising administering an adjuvant, boost, or facilitating agent before, during, or after administration of the composition.
35. The method of claim 31, wherein the vertebrate mammal is a mouse, a rat, a rabbit, a non-human primate, or a human.

36. The method of claim 31, wherein the mode of administration is topical administration, oral administration, injection by needle, needleless jet injection, intramuscular administration, intradermal administration, and gene gun administration.
37. The method of claim 31, wherein the distinct clades are any two or more of A, B, C, D, E, F, G, H, I, J, and K.
38. The method of claim 31, wherein the vertebrate mammal is a human.
39. The method of claim 38, wherein the human is at risk for, or infected with human immunodeficiency virus.
40. An isolated protein composition comprising a set of isolated human immunodeficiency virus (HIV) envelope glycoprotein molecules, wherein each molecule in the set comprises a primary isolate sequence.
41. A protein composition comprising a plurality of sets of isolated human immunodeficiency virus (HIV) envelope glycoprotein molecules, wherein each molecule in the sets comprises a different type of HIV envelope glycoprotein, or comprises a primary isolate sequence from a distinct genetic clade.
42. The composition of claim 41, wherein the envelope glycoprotein of one or more of the plurality of sets is a HIV-1 envelope glycoprotein.
43. The composition of claim 41, wherein the envelope glycoprotein of each set is selected from the group consisting of gp120, gp140, gp160, and gp41.
44. The composition of claim 43, wherein the envelope glycoprotein of one or more of the plurality of sets is a gp120 envelope glycoprotein.

45. The composition of claim 41, wherein the envelope glycoprotein of one or more of the plurality of sets is from a clade of a major (M) group of clades.

46. The composition of claim 45, wherein the clade is clade A, B, C, D, E, F, G, H, I, J, or K.

47. The composition of claim 41, wherein the envelope glycoprotein of one or more of the plurality of sets is from a clade of an outlier (O) group of clades.

48. The composition of claim 41, wherein the envelope glycoprotein of one or more of the plurality of sets is from a clade of an N group of clades.

49. The composition of claim 48, wherein the clade is clade B.

50. The composition of claim 41, wherein the envelope glycoprotein is an envelope glycoprotein of a B715 isolate.

51. The composition of claim 41, wherein the clade is clade C.

52. The composition of claim 41, further comprising a pharmaceutically acceptable excipient to form a pharmaceutical composition.

53. A method of treating an individual with Acquired Immune Deficiency Syndrome (AIDS), the method comprising, administering to the individual an amount of the pharmaceutical composition of claim 52 sufficient to induce inhibit disease progression due to human immunodeficiency virus (HIV).

54. A method of inducing an immune response against human immunodeficiency virus (HIV) or a HIV epitope in a vertebrate mammal, the method comprising :  
administering to the mammal the nucleic acid composition of claim 30;

administering to the mammal the protein composition of claim 52; wherein the nucleic acid composition and the protein composition are administered in amounts sufficient to elicit a detectable immune response against HIV or an HIV epitope in the vertebrate mammal.

55. The method of claim 54, further comprising isolating immune cells from the vertebrate mammal; and testing an immune response of the isolated immune cells in vitro.

56. The method of claim 54, wherein the protein composition is administered after the nucleic acid composition.

57. The method of claim 56, wherein the protein composition is administered between 4 and 8 weeks after the nucleic acid composition.

58. The method of claim 54, wherein a cell-mediated immune response is tested.

59. The method of claim 54, wherein a humoral immune response is tested.

60. The method of claim 59, wherein a neutralizing humoral response is tested.

61. A kit comprising:

a nucleic acid composition of claim 1, and instructions for administering the nucleic acid composition to an individual.

62. The kit of claim 61, further comprising a protein composition comprising a set of isolated human immunodeficiency virus (HIV) envelope glycoprotein molecules.

63. The kit of claim 61, wherein the kit further comprises one or more additional sets of isolated HIV envelope glycoproteins, wherein each set is a different type of HIV envelope glycoprotein, or comprises a primary isolate sequence from a distinct genetic clade.

64. The kit of claim 61, wherein one or more of the HIV envelope glycoproteins encoded by the nucleic acid molecules of the nucleic acid composition is of a same type or clade as one or more of the envelope glycoproteins of the protein composition.

65. The kit of claim 64, wherein each of the HIV envelope glycoproteins encoded by the sets of nucleic acid molecules of the nucleic acid composition is of a same type or clade as each of the envelope glycoproteins of the protein composition.

66. A kit comprising:

a protein composition comprising a set of isolated human immunodeficiency virus (HIV) envelope glycoprotein molecules, wherein each set comprises a different type of HIV envelope glycoprotein, or comprises a primary isolate sequence from a distinct genetic clade; and

instructions for administration of the composition to an individual that has been administered an HIV vaccine.

67. The kit of claim 66, wherein the individual has been administered a nucleic acid HIV vaccine.

68. The kit of claim 66, wherein the protein composition further comprises an excipient.

69. The kit of claim 68, wherein the excipient is cyclodextrin.

70. The kit of claim 66, wherein the protein composition further comprises an adjuvant.

71. The kit of claim 70, wherein the adjuvant is QS-21.

72. The kit of claim 61, wherein the kit further comprises instructions for administration to an individual according to a method, the method comprising:

administering the nucleic acid composition to the individual, and administering a protein composition comprising a set of isolated human immunodeficiency virus (HIV)



envelope glycoprotein molecules to the individual, wherein the protein composition is administered after the nucleic acid composition.

73. The kit of claim 72, wherein the individual is a mammal.

74. The kit of claim 73, wherein the mammal is a human.

75. The kit of claim 72, wherein the protein composition further comprises one or more additional sets of isolated HIV envelope glycoproteins, wherein each set is a different type of HIV envelope glycoprotein, or comprises a primary isolate sequence from a distinct genetic clade.

76. The kit of claim 75, wherein the nucleic acid composition is administered to the individual two or more times.

77. The kit of claim 75, wherein the protein composition is administered to the individual two or more times.

78. The kit of claim 61, further comprising instructions for administration to an individual according to a method, the method comprising: administering the nucleic acid composition to the individual, and administering the protein composition to the individual, wherein the protein composition is administered after the nucleic acid composition.

79. The kit of claim 78, wherein the individual is a mammal.

80. The kit of claim 79, wherein the mammal is a human.